=> d l1; d his; log y L1 HAS NO ANSWERS L1 STR

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

Structure attributes must be viewed using STN Express query preparation.

(FILE 'HOME' ENTERED AT 15:40:12 ON 23 JUL 2003)

FILE 'REGISTRY' ENTERED AT 15:40:32 ON 23 JUL 2003

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 7 S L1 FUL

FILE 'CAPLUS' ENTERED AT 15:41:11 ON 23 JUL 2003

L4 3 S L3

FILE 'BEILSTEIN' ENTERED AT 15:41:47 ON 23 JUL 2003

L5 2 S L1 FUL

L6 2 S L5 NOT L4

FILE 'MARPAT' ENTERED AT 15:42:32 ON 23 JUL 2003

L7 0 S L1

L8 2 S L1 FUL

L9 0 S L8 NOT L4

COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 104.55 325.73

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL
ENTRY SESSION
CA SUBSCRIBER PRICE

0.00 -1.95

STN INTERNATIONAL LOGOFF AT 15:43:08 ON 23 JUL 2003

C:\Program Files\Stnexp\Queries\10019804.str

```
ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
L4
ΑN
     2002:487542 CAPLUS
     137:63247
DN
ΤI
     Preparation of quaternized N-aminoalkyldioxobenzothiazine-3-carboxamides
     for treatment of cartilage disorders
     Madelmont, Jean-Claude; Giraud, Isabelle; Vidal, Aurelien; Mounetou,
IN
     Emmanuelle; Rapp, Maryse; Maurizis, Jean-Claude; Renard, Pierre;
     Caignard, Daniel-Henri; Bizot-Espiard, Jean-Guy
PA
     Les Laboratoires Servier, Fr.; Institut National De La Recherche
     Medicale
SO
     PCT Int. Appl., 38 pp.
     CODEN: PIXXD2
DT
     Patent
     French
LA
FAN.CNT 1
     PATENT NO.
                      KIND
                                            APPLICATION NO.
                            DATE
                                                             DATE
PΙ
     WO 2002050049
                       A1
                            20020627
                                            WO 2001-FR4135
                                                             20011221
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, TR
     FR 2818641
                            20020628
                                            FR 2000-16739
                       A1
                                                             20001221
     AU 2002028120
                       Α5
                            20020701
                                            AU 2002-28120
                                                             20011221
PRAI FR 2000-16739
                       Α
                            20001221
     WO 2001-FR4135
                       W
                            20011221
     CASREACT 137:63247; MARPAT 137:63247
OS
GΙ
        R1
```

$$\begin{array}{c|c}
R1 & 0 \\
\hline
\\
R2
\end{array}$$

AB Title compds. [(un)substituted I; R = NHZNR5R6R7X; R1 = H, OH, alkoxy, etc.; R2 = H or alkyl; R5-R7 = alkyl or 2 of R5-R7 = atoms to complete a ring and the other = alkyl; X = halo; Z = alkylene; dashed line = optional addnl. bond] were prepd. Thus, I (R1 = OH, R2 = Me)(II; R = OMe) was amidated by H2N(CH2)3NEt2 and the product quaternized to give II [R = NH(CH2)3NMEEt2I]. Data for biol. activity of I were given.

TT 439254-42-9P 439254-44-1P 439254-46-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of quaternized N-aminoalkyldioxobenzothiazine-3-carboxamides for treatment of cartilage disorders)

RN 439254-42-9 CAPLUS

CN 1-Propanaminium, N,N-diethyl-3-[[(4-hydroxy-2-methyl-1,1-dioxido-2H-1,2-benzothiazin-3-yl)carbonyl]amino]-N-methyl-, iodide (9CI) (CA INDEX NAME)

• I -

RN 439254-44-1 CAPLUS

CN 1-Propanaminium, N,N,N-triethyl-3-[[(4-hydroxy-2-methyl-1,1-dioxido-2H-1,2-benzothiazin-3-yl)carbonyl]amino]-, iodide (9CI) (CA INDEX NAME)

• I-

RN 439254-46-3 CAPLUS

CN 1-Butanaminium, 4-[[(4-hydroxy-2-methyl-1,1-dioxido-2H-1,2-benzothiazin-3-yl)carbonyl]amino]-N,N,N-trimethyl-, iodide (9CI) (CA INDEX NAME)

•.I-

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

Appis

```
L4
    ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ΑN
     2001:12454 CAPLUS
DN
     134:71584
TI
    Novel quaternary ammonium derivatives, method for preparing same and
    pharmaceutical use for treatment or diagnosis of pathologies affecting
IN
    Madelmont, Jean-claude; Giraud, Isabelle; Nicolas, Colette; Maurizis,
     Jean-claude; Rapp, Maryse; Ollier, Monique; Renard, Pierre; Caignard,
     Daniel-henri
    Adir Et Compagnie, Fr.
PA
SO
    PCT Int. Appl., 34 pp.
    CODEN: PIXXD2
DT
     Patent
    French
LΑ
FAN.CNT 1
    PATENT NO.
                     KIND
                            DATE
                                           APPLICATION NO.
                                                            DATE
                                           -----
    WO 2001000621
                      A1
                            20010104
                                           WO 2000-FR1731
                                                            20000622
ΡI
            AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
             DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
             JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
            MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
             TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
            MD, RU, TJ, TM
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
            PT. SE
    FR 2795412
                            20001229
                                           FR 1999-8020
                      A1
                                                            19990623
    FR 2795412
                            20010713
                       В1
    EP 1185526
                      A1
                            20020313
                                           EP 2000-945979
                                                            20000622
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
    BR 2000011943
                            20020514
                                           BR 2000-11943
                      Α
                                                            20000622
    JP 2003503407
                       T2
                            20030128
                                           JP 2001-507029
                                                            20000622
    NO 2001006267
                       Α
                            20020130
                                           NO 2001-6267
                                                            20011220
PRAI FR 1999-8020
                      Α
                            19990623
                      W
                            20000622
    WO 2000-FR1731
OS
    MARPAT 134:71584
AΒ
    The invention concerns compds. [M-(X)n-N+R1R2R3]Hal- (Ia) wherein M=a
    mol. for use in the treatment or diagnosis of pathologies affecting
    cartilage; R1, R2, R3 = alkyl group, or R1, R2, R3 together with the N
    atom which bears them form a heterocycle; X = C1-C6 alkyl chain wherein
    one or several -CH2- groups are optionally substituted by S, O, -NR, -
    CO-, -CO-NH-, -CO2-, SO- or SO2- group; n=0 or 1; Hal-= halide, or
     [(A)(B)(C)N+R4]Hal-(Ib) in which R4 = linear or branched C1-6 alkyl
    groups, Hal- = halide, and general formula (A)(B)(C)N (F1) represents a
    mol. for use in the treatment or diagnosis of pathologies affecting
    cartilage, provided that the N atom can optionally be included in a
    satd. or unsatd. nitrogenous heterocyclic system, or involved in a
    double bond. Pathologies of cartilage affected by treatment with compds.
    Ia and Ib may include use as anti-inflammatories, analgesics, anti-
    osteoarthritics, antiarthritics, and antitumor agents. More specific
    structures for [M-(X)n-N+R1R2R3]Hal- (Ia) are also claimed where M=
    derivs. of Tenidap, Melphalan, Chlorambucil, or glucosamine, and for
     structure Ib which includes Piroxicam derivs. A dioxotechnetium complex
```

of a 1,4,7,10,13-pentaazacyclopentadecane deriv. is also claimed and a prepn. is given. Processes for the prepn. of the compds. are also

claimed and

example prepns. are provided, e.g., via a peptide coupling reaction. IT 256419-19-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. and use of quaternary ammonium halides for treatment or diagnosis of pathologies affecting cartilage, and biodistribution in rat)

RN 256419-19-9 CAPLUS

CN 1-Propanaminium, 3-[[(4-hydroxy-2-methyl-1,1-dioxido-2H-1,2-benzothiazin-3-yl)carbonyl]amino]-N,N,N-trimethyl-, iodide (9CI) (CA INDEX NAME)

• 1-

IT 256419-17-7P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and use of quaternary ammonium halides for treatment or diagnosis of pathologies affecting cartilage, and biodistribution in rat)

RN 256419-17-7 CAPLUS

CN Pyridinium, 2-[[(4-hydroxy-2-methyl-1,1-dioxido-2H-1,2-benzothiazin-3-yl)carbonyl]amino]-1-methyl-, iodide (9CI) (CA INDEX NAME)

• I-

Committee of the second

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1999:757962 CAPLUS

DN 132:117300

TI New Quaternary Ammonium Oxicam Derivatives Targeted toward Cartilage: Synthesis, Pharmacokinetic Studies, and Antiinflammatory Potency

AU Nicolas, Colette; Verny, Michel; Giraud, Isabelle; Ollier, Monique; Rapp, Maryse; Maurizis, Jean-Claude; Madelmont, Jean-Claude

CS INSERM Unite 484, Clermont-Ferrand, 63005, Fr.

SO Journal of Medicinal Chemistry (1999), 42(25), 5235-5240 CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

AB Analogs of nonsteroidal antiinflammatory drugs (NSAIDs) oxicams, in which the active group was linked to a quaternary ammonium function [(4-hydroxy-2-methyl-2H-1,2-benzothiazine-1,1-dioxide-3-carboxamido)2methylpyridinium iodide or piroxicam-N+ and [3-(4-hydroxy-2-methyl-2H-1,2-benzothiazine-1,1-dioxide-3-carboxamido)propyl]trimethylammonium iodide or propoxicam-N+] were synthesized. Compds. were labeled with tritium for piroxicam-N+ and carbon-14 for propoxicam-N+. Pharmacokinetic studies conducted on rats showed that these mols. were able to highly conc. in joint cartilages but their bioavailability by the oral route was low. Only propoxicam-N+ exhibited a sufficient water soly. to be administered i.v. This mol. was able to restore proteoglycans biosynthesis in cultured articular chondrocytes treated with Interleukin-1.beta. with an efficiency identical to that of indomethacin. These results suggest that the functionalization of oxicam derivs. by a quaternary ammonium group greatly increases their affinity toward articular cartilage without eliminating their pharmacol. activity. New drugs synthesized according to this scheme could be useful to obtain a significant decrease of the efficient administered dose and consequently an attenuation of adverse effects such as digestive toxicity.

IT 256419-17-7 256419-19-9

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (new quaternary ammonium oxicam derivs. targeted toward cartilage in relation to synthesis and pharmacokinetic studies and antiinflammatory potency detd. as inhibition of proteoglycan synthesis)

RN 256419-17-7 CAPLUS

CN Pyridinium, 2-[[(4-hydroxy-2-methyl-1,1-dioxido-2H-1,2-benzothiazin-3-yl)carbonyl]amino]-1-methyl-, iodide (9CI) (CA INDEX NAME)

• I -

RN 256419-19-9 CAPLUS

CN 1-Propanaminium, 3-[[(4-hydroxy-2-methyl-1,1-dioxido-2H-1,2-benzothiazin-3-yl)carbonyl]amino]-N,N,N-trimethyl-, iodide (9CI) (CA

INDEX NAME)

RN

• ı -

IT 256419-26-8P 256419-32-6P

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process) (new quaternary ammonium oxicam derivs. targeted toward cartilage in relation to synthesis and pharmacokinetic studies and antiinflammatory potency detd. as inhibition of proteoglycan synthesis) 256419-26-8 CAPLUS

CN Pyridinium, 2-[[[4-hydroxy-2-(methyl-t3)-1,1-dioxido-2H-1,2-benzothiazin-3-yl]carbonyl]amino]-1-methyl-, iodide (9CI) (CA INDEX NAME)

• I-

RN 256419-32-6 CAPLUS

CN 1-Propanaminium, 3-[[(4-hydroxy-2-methyl-1,1-dioxido-2H-1,2-benzothiazin-3-yl)carbonyl-14C]amino]-N,N,N-trimethyl-, iodide (9CI) (CA INDEX NAME)

• I-

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

CM 2

FBRN 3587184 FMF I

Reference(s):

 Nicolas, Colette; Verny, Michel; Giraud, Isabelle; Ollier, Monique; Rapp, Maryse; Maurizis, Jean-Claude; Madelmont, Jean-Claude, J.Med.Chem., CODEN: JMCMAR, 42(25), <1999>, 5235 - 5240; BABS-6228165

Reference (s):

1. Reymond, Frederic; Steyaert, Guillaume; Pagliara, Alessandra; Carrupt, Pierre-Alain; Testa, Bernard; Girault, Hubert, Helv.Chim.Acta, CODEN: HCACAV, 79(6), <1996>, 1651-1669; BABS-6020103

```
L5 ANSWER 1 OF 1 MARPAT COPYRIGHT 2003 ACS on STN
```

AN 137:63247 MARPAT

TI Preparation of quaternized N-aminoalkyldioxobenzothiazine-3-carboxamides for treatment of cartilage disorders

PA Les Laboratoires Servier, Fr.; Institut National De La Recherche Medicale

SO PCT Int. Appl., 38 pp. CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

	PATENT NO.		KIND DATE			APPLICATION NO.			٥.	DATE								
PI	WO 2002050049		A1 20020627			WO 2001-FR4135			- - 5	2001	 1221							
		W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
			CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
															KZ,			
															NO,			
			PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,
			UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZM,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,
			ТJ,	TM														
		RW:	AT,	BE,	CH,	CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,
			PT,	SE,	TR													
	FR 2818641		A1 20020628			FR 2000-16739 20			2000	20001221								
	AU 2002028120 A5		5	20020701			AU 2002-28120				20011221							
PRAI	AI FR 2000-16739 200012			0012	21													
	WO	2001	-FR4	135	20	0112	21											
os	CASREACT 137:63247																	
GI																		

$$\begin{array}{c|c}
R1 & 0 \\
\downarrow & \parallel \\
0 & S \leq N \\
R2
\end{array}$$

AB Title compds. [(un)substituted I; R = NHZNR5R6R7X; R1 = H, OH, alkoxy, etc.; R2 = H or alkyl; R5-R7 = alkyl or 2 of R5-R7 = atoms to complete a ring and the other = alkyl; X = halo; Z = alkylene; dashed line = optional addnl. bond] were prepd. Thus, I (R1 = OH, R2 = Me)(II; R = OMe) was amidated by H2N(CH2)3NEt2 and the product quaternized to give II [R = NH(CH2)3NMeEt2I]. Data for biol. activity of I were given.

MSTR 1

G3 = OH

G6 = alkylene < (1-6) >

G7 = 26

G8 = alkyl<(1-6)> G10 = alkyl<(1-6)>

MPL: claim 1

NTE: substitution is restricted

STE: and isomers

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 11; d his; log y L1 HAS NO ANSWERS L1 STR

~ a . F

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

Structure attributes must be viewed using STN Express query preparation.

(FILE 'HOME' ENTERED AT 15:36:29 ON 23 JUL 2003)

FILE 'REGISTRY' ENTERED AT 15:36:36 ON 23 JUL 2003

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 0 S L1 FUL

FILE 'MARPAT' ENTERED AT 15:37:02 ON 23 JUL 2003

L4 0 S L1

L5 1 S L1 FUL

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	108.78	257.14
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-0.62	-0.62

STN INTERNATIONAL LOGOFF AT 15:37:46 ON 23 JUL 2003

L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2003:26751 CAPLUS

DN 138:368857

TI Synthesis of 3-aminohydantoinyl-1,2-benzothiazine derivatives

AU Park, Myung-Sook; Chang, Eun-Sung; Lee, Myung-Sook; Kwon, Soon-Kyoung

CS College of Pharmacy, Duksung Women's University, Seoul, 132-714, S. Korea

SO Bulletin of the Korean Chemical Society (2002), 23(12), 1836-1838 CODEN: BKCSDE; ISSN: 0253-2964

PB Korean Chemical Society

DT Journal

LA English

GI

AB N-dioxoimidazolidinyl hydroxybenzothiazinecarboxamides I (R = EtCH2, Bu, Me2CH, Me2CHCH2; R1 = H, Br, C1) are prepd. as potential analgesic and antiinflammatory agents. 5-Substituted 3-aminoimidazolidinediones (3-aminohydantoins) are prepd. by cyclocondensation of L-amino acids and tert-Bu carbazate in quinoline. Alkylation of the sodium salts of saccharins II (R1 = H, Br, C1) with Me chloroacetate followed by ring expansion in the presence of sodium methoxide in methanol gives dioxobenzothiazinecarboxylates III (R1 = H, Br, C1). Amidation of III (R1 = H, Br, C1) with 5-substituted 3-aminohydantoins provides the title compds. I (R = EtCH2, Bu, Me2CH, Me2CHCH2; R1 = H, Br, C1) in three steps from saccharins II. I (R = EtCH2, Bu, Me2CH, Me2CHCH2; R1 = H, Br, C1) show analgesic and antiinflammatory activities (no data).

Ι

IT 524707-42-4P 524707-44-6P 524707-46-8P 524707-48-0P 524707-50-4P 524707-52-6P 524707-54-8P 524707-56-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. of N-dioxoimidazolidinyl dioxobenzothiazinecarboxamides from saccharin sodium salts and 3-aminohydantoins and their potential analgesic and antiinflammatory activities)

RN 524707-42-4 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-chloro-N-(2,5-dioxo-4-propyl-1-imidazolidinyl)-4-hydroxy-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 524707-44-6 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, N-(4-butyl-2,5-dioxo-1-imidazolidinyl)-

7-chloro-4-hydroxy-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 524707-46-8 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-chloro-4-hydroxy-N-[4-(1-methylethyl)-2,5-dioxo-1-imidazolidinyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 524707-48-0 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-chloro-4-hydroxy-N-[4-(2-methylpropyl)-2,5-dioxo-1-imidazolidinyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 524707-50-4 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-bromo-N-(2,5-dioxo-4-propyl-1-imidazolidinyl)-4-hydroxy-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 524707-52-6 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-bromo-N-(4-butyl-2,5-dioxo-1-imidazolidinyl)-4-hydroxy-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 524707-54-8 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-bromo-4-hydroxy-N-[4-(1-methylethyl)-

2,5-dioxo-1-imidazolidinyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 524707-56-0 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-bromo-4-hydroxy-N-[4-(2-methylpropyl)-2,5-dioxo-1-imidazolidinyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
AN
     2000:654165 CAPLUS
DN
     133:358999
ΤI
     Studies on synthetic 1,2-benzothiazine anti-inflammatory agents:
     pharmacological effect and the expression of xenobiotic-metabolizing
ΑU
     Kim, Sang Geon; Cho, Joo Youn; Kwon, Soon-Kyung; Lee, Eun Bang
CS
     College of Pharmacy, Seoul National University, S. Korea
SO
     Yakhak Hoechi (2000), 44(4), 300-307
     CODEN: YAHOA3; ISSN: 0513-4234
PB
     Pharmaceutical Society of Korea
DT
     Journal
LΑ
     Korean
AB
     Expression of xenobiotic-metabolizing enzymes can be altered by
     xenobiotics, which represent changes in the prodn. of reactive metabolic
     intermediates as well as toxicities in tissues. Metabolic intermediates
     derived from xenobiotics are considered to produce the reactive oxygen
     species including drug free radicals and hydroxyl free radicals, which
     would be ultimately responsible for drug-induced toxicities. The
effects
     of 1,2-benzothiazine anti-inflammatory agents on the expression of
     xenobiotic-metabolizing enzymes including major cytochrome P450s,
     microsomal epoxide hydrolase (mEH) and glutathione S-transferase (GST)
     were studied in the liver with the aim of providing the part of
     information on potential prodn. of reactive metabolites and
hepatotoxicity
     by the agents. The synthetic compds. 7-bromo-4-hydroxy-N-[4-oxo-3-(2-
     propenyl)-2-thioxo-1-imidazolidinyl]-2H-1,2-benzothiazine-3-carboxamide-
     1,1-dioxide (I), 7-bromo-N-[3-(4-chlorophenyl)-4-oxo-2-thioxo-1-
     imidazolidinyl]-4-hydroxy-2-(2-propenyl)-2H-1,2-benzothiazine-3-
     carboxamide-1,1-dioxide, and 7-chloro-4-hydroxy-N-[4-oxo-3-(2-propenyl)-
2-
     thioxo-1-imidazolidinyl]-2H-1,2-benzothiazine-3-carboxamide-1,1-dioxide
     (II) exhibited anti-inflammatory effects in rats as assessed by the
     Randall-Selitto method. The anti-inflammatory effect was detected as
     early as at 30 min after gavaging the agents with the ED50 being noted
at
     80 mg/kg, which was comparable to that of ibuprofen. Treatment of rats
     with each compd. (100 mg/kg, 3d) resulted in no significant induction in
     the immunochem.-detectable cytochromes P 450 1A1/2, P 450 2B1/2, P 450
     2C11 and P 450 2E1. Changes in the mEH expression were also minimal, as
     evidenced by both Western blot and Northern blot analyses. Hepatic GST
     expression was slightly increased by the agents: GST Ya protein and mRNA
     expression was .apprx.1.5-fold increased after treatment with compds. I
     and II, whereas GST Yb1/2 and Yc1/2 mRNA levels were elevated 2- to
     3-fold. In summary, the effects of the synthetic 1,2-benzothiazines on
     the expression of major P 450, mEH and GST were not significant,
providing
     evidence that metabolic activation of the agents, potential drug
     interaction and hepatotoxicity would be minimal.
     183859-52-1 183859-65-6
     RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
     study, unclassified); BIOL (Biological study)
        (effects of benzothiazine anti-inflammatory agents on expression of
        xenobiotic-metabolizing enzymes)
RN
     183859-52-1 CAPLUS
```

ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN

L4

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-bromo-4-hydroxy-N-[4-oxo-3-(2-propenyl)-2-thioxo-1-imidazolidinyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 183859-65-6 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-chloro-4-hydroxy-N-[4-oxo-3-(2-propenyl)-2-thioxo-1-imidazolidinyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1999:201272 CAPLUS

DN 130:338076

TI Synthesis and analgesic and anti-inflammatory activities of 1,2-benzothiazine derivatives

AU Lee, Eun Bang; Kwon, Soon Kyoung; Kim, Sang Geon

CS Natural Products Research Institute, Seoul National University, Seoul, 110-460, S. Korea

SO Archives of Pharmacal Research (1999), 22(1), 44-47 CODEN: APHRDQ; ISSN: 0253-6269

Ι

PB Pharmaceutical Society of Korea

DT Journal

LA English

GI

AB Three 1,2-benzothiazine derivs. I (R = H, R' = allyl, X = Cl, Br; R = allyl, R' = 4-ClC6H4, X = Br) were synthesized, and their analgesic/anti-inflammatory efficacy and their effects on gastric irritation were evaluated. Among the three compds., I (R = H, R' = allyl, X = Cl) exhibited the most potent analgesic action, but the effect was weaker than that of piroxicam. Nonetheless, the compd. showed 4 times more potent analgesic action with less gastric damage than did ibuprofen. These compds. did not show anti-inflammatory effect at an oral dose of 5 mg/kg.

IT 183859-52-1P 183859-65-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation) (prepn., analgesic, and anti-inflammatory activity of benzothiazines)

RN 183859-52-1 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-bromo-4-hydroxy-N-[4-oxo-3-(2-propenyl)-2-thioxo-1-imidazolidinyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 183859-65-6 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-chloro-4-hydroxy-N-[4-oxo-3-(2-propenyl)-2-thioxo-1-imidazolidinyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1997:55223 CAPLUS

DN 126:264061

TI Studies on the activities and synthesis of N-substituted pyrimidinyl or triazinyl-3-carbamoyl-4-hydroxy-2H-1,2-benzothiazine-1,1-dioxides

AU Zhao, Guo-Feng; Zou, Xiao-Mao; Yang, Hua-Zheng

CS Inst. Elemento-Organic Chem. Nankai Univ., Tianjin, 300071, Peop. Rep. China

SO Gaodeng Xuexiao Huaxue Xuebao (1996), 17(10), 1560-1564 CODEN: KTHPDM; ISSN: 0251-0790

Ι

PB Gaodeng Jiaoyu Chubanshe

DT Journal

LA Chinese

GΙ

AB Title compds. I(R = H, Me; R1, R2 = MeO, C1, Me) were prepd. by aminolysis of 4-hydroxy-2-hydro(methyl)-2H-1,2-benzothiazine-3-carboxylic acid Et ester 1,1-dioxides with substituted aminopyrimidines or aminotriazines. Their structures were characterized by 1H NMR, IR, MS and elementary anal. The biol. tests indicated that the majority of these compds. showed herbicidal activity and some showed plant-growth regulating activity and antiinflammatory activity.

IT 186695-73-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological $\,$

RN 186695-73-8 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, N-(4-chloro-6-methoxy-2-pyrimidinyl)-4-

hydroxy-, 1,1-dioxide (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} OH & O \\ \hline \\ O & NH \\ \hline \\ O & C1 \\ \end{array}$$

L4ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN AN 1996:664323 CAPLUS DN 126:1096 Some new 1,2-benzothiazine derivatives with analgesic and ΤI anti-inflammatory activities ΑU Kwon, Soon Kyoung; Park, Myung Sook College Pharmacy, Duk-Sung Women's University, Seoul, 132-714, S. Korea CS SO Arzneimittel-Forschung (1996), 46(10), 966-971 CODEN: ARZNAD; ISSN: 0004-4172 PB Cantor DTJournal LΑ English AB Twenty-three new 7-halo-4-hydroxy 2H(or alkyl)-N-(3-aralkyl-2-thio-1hydantoinyl)-2H-1,2-benyothiazine-3-carboxamide 1,1-dioxide derivs. were synthesized through the condensation of 7-halo-4-hydroxy-2H(or alkyl)-1,2-benzothiazine-3-carboxylic acid Me ester 1,1-dioxides with 1-amino-2-thio-3-aralkylimidazolidine-4-ones. The analgesic and anti-inflammatory activities of the synthesized compds. were investigated by acetic acid-induced writhing syndrome and carrageenan rat paw edema tests. In analgesic activities most compds. exhibited higher activities than acetylsalicylic acid, but in anti-inflammatory activities most compds. except 3 of them showed lower activities than indomethacin. 183859-51-0P 183859-52-1P 183859-54-3P 183859-55-4P 183859-64-5P 183859-65-6P 183859-66-7P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. and analgesic and anti-inflammatory activities of benzothiazine derivs.) 183859-51-0 CAPLUS RN CN 2H-1,2-Benzothiazine-3-carboxamide, 7-bromo-4-hydroxy-N-(3-methyl-4-oxo-2thioxo-1-imidazolidinyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 183859-52-1 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-bromo-4-hydroxy-N-[4-oxo-3-(2-propenyl)-2-thioxo-1-imidazolidinyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 183859-54-3 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-bromo-N-[3-(4-chlorophenyl)-4-oxo-

2-

thioxo-1-imidazolidinyl]-4-hydroxy-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 183859-55-4 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-bromo-4-hydroxy-N-[4-oxo-3-(phenylmethyl)-2-thioxo-1-imidazolidinyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 183859-64-5 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-chloro-4-hydroxy-N-(3-methyl-4-oxo-2-

thioxo-1-imidazolidinyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 183859-65-6 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-chloro-4-hydroxy-N-[4-oxo-3-(2-propenyl)-2-thioxo-1-imidazolidinyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

RN 183859-66-7 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, 7-chloro-4-hydroxy-N-(4-oxo-3-phenyl-2-

thioxo-1-imidazolidinyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1993:449321 CAPLUS

DN 119:49321

TI The synthesis of 1,2-benzothiazine-3-carboxamidylhydantoin derivatives and their antiinflammatory and analgesic activities

AU Kwon, Soon Kyoung; Park, Myoung Suk

CS Coll. Pharm., Duksung Women's Univ., Seoul, 132-714, S. Korea

SO Archives of Pharmacal Research (1992), 15(3), 251-5 CODEN: APHRDO; ISSN: 0253-6269

DT Journal

LA English

OS CASREACT 119:49321

GI

AB Twenty-one 4-hydroxy-2H (or alkyl)-N-(3-aralkyl-2-thio-1-hydantoinyl)1,2-benzothiazine-3-carboxamide 1,1-dioxides, e.g., I, were synthesized through the reaction of 4-hydroxy-2H (or alkyl)-1,2-benzothiazine-3carboxylic Me ester 1,1-dioxides and 1-amino-2-thio-3-aralkyl-4imidazolones in xylene. The compds. synthesized were screened for antiinflammatory effect on carrageenin-induced edema in rat and for analgesic effect on acetic acid-induced writhing syndrome in mice. Most compds. were inhibitors of carrageenin-induced rat foot edema and some showed significant antiinflammatory activity comparable to that of indomethacin and significant analgesic activity comparable to that of indomethacin and aspirin.

IT 148316-43-2P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn., antiinflammatory and analgesic activity of)

RN 148316-43-2 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, N-[3-(4-chlorophenyl)-4-oxo-2-thioxo-1-imidazolidinyl]-4-hydroxy-, 1,1-dioxide (9CI) (CA INDEX NAME)

```
L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
```

AN 1984:472742 CAPLUS

DN 101:72742

TI 4-Hydroxy-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide, its use, and pharmaceuticals containing these compounds

IN Trummlitz, Guenter; Engel, Wolfhard; Seeger, Ernst; Haarmann, Walter

PA Thomae, Dr. Karl, G.m.b.H., Fed. Rep. Ger.

SO Ger. Offen., 32 pp. CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.			KIND	DATE	AP	DATE		
ΡI	DE	 3237473		A1	19840412	DE.	1982-3237473	19821009	
	ΕP	106214		A1			1983-109512		
	ΕP	106214		В1	19851204		1000 100012	13000321	
		R: AT,	BE,		FR, IT,	LU,	NL, SE		
	AT	16807		E			1983-109512	19830924	
	US	4533664		Α			1983-537592	19830930	
	FΙ	8303566		A			1983-3566	19831003	
	SU	1148565		A 3	19850330	SU	1983-3654490	19831005	
	DK	8304607		Α	19840410	DK	1983-4607	19831006	
	DD	215549		A 5	19841114	DD	1983-255478	19831006	
	NO	8303665		Α	19840410		1983-3665	19831007	
	ΑU	8319986		A1	19840412		1983-19986	19831007	
	GB	2128190		A1	19840426	GB	1983-26876	19831007	
	GB	2128190		B2	19860702				
	JP	59088482		A2	19840522	JP	1983-188284	19831007	
	ES	526332		A1	19841116	ES	1983-526332	19831007	
	HU	34472		A2	19850328	HU	1983-3482	19831007	
	HU	190169		В	19860828				
	CS	236896		B2	19850515	CS	1983-7378	19831007	
	ZA	8307500		Α	19850626	ZA	1983-7500	19831007	
	CA	1207767		A1	19860715	CA	1983-438617	19831007	
	PL	139147		B1	19861231	\mathtt{PL}	1983-244080	19831007	
	IL	69931		A1	19870331	IL	1983-69931	19831007	
	ES	531402		A 1	19841216	ES	1984-531402	19840409	
PRAI	DE	1982-3237	473		19821009				
	EP	1983-1095	12		19830924				
os	CAS	SREACT 101	.:727	742					
GI									

AB The title compds. (I; R = H, Me, MeO, Cl, F; R1 = H, Me, Et, Pr) were prepd. Thus, Me 4-hydroxy-2-methyl-2H-1,2-benzothiazine-3-carboxylate 1,1-dioxide was refluxed 24 h in C6H4Me2 with 2-amino-6-chloropyrazine to give 64% I (R = H, R1 = Me) (II). In mice 10 mg II/kg orally increased bleeding time 103%.

IT 91286-70-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn., ethylation, and methylation of)

RN 91286-70-3 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, N-(6-chloropyrazinyl)-4-hydroxy-, 1,1-dioxide (9CI) (CA INDEX NAME)

L4 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1975:472175 CAPLUS

DN 83:72175

TI Benzothiazine dioxides as antithrombotic agents

IN Lombardino, Joseph G.; Wiseman, Edward A.

PA Pfizer, Inc.

SO U.S., 6 pp. CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
PI	US 3862319	Α	19750121	US 1973-362518	19730521		
PRAI	US 1969-829713		19690602				
	US 1971-114037		19710209				

GI For diagram(s), see printed CA Issue.

AB Compds. of the general structures I and II were effective antithrombotic agents. Physiol. testing data in animals and man was given.

IT 56209-19-9

RL: BIOL (Biological study)
 (antithrombotic)

RN 56209-19-9 CAPLUS

CN 2H-1,2-Benzothiazine-3-carboxamide, N-(5-chloro-2-pyridinyl)-3,4-dihydro-4-hydroxy-2-methyl-, 1,1-dioxide (9CI) (CA INDEX NAME)

Reference(s):

Beilstein Records (BRN): Molec. Formula (MF): 7784248 C19 H15 Br N4 O5 S2

Molecular Weight (MW):

523.38

Lawson Number (LN):

31458, 28769, 14140

Compound Type (CTYPE):
Constitution ID (CONSID):

heterocyclic 6631776 7358730

Tautomer ID (TAUTID):
Beilstein Citation (BSO):

6-27

Entry Date (DED):
Update Date (DUPD):

1998/03/03 1998/03/03

Reference(s):

Molec. Formula (MF): C18 H13 Br N4 O5 S2

Molecular Weight (MW): 509.35

Lawson Number (LN): 31458, 28769, 14131

Compound Type (CTYPE): heterocyclic

Constitution ID (CONSID): 6629621
Tautomer ID (TAUTID): 7358136
Beilstein Citation (BSO): 6-27

Entry Date (DED): 1998/03/03 Update Date (DUPD): 1998/03/03

Reference(s):

L8 ANSWER 4 OF 8 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL on STN

Beilstein Records (BRN): 7783308

Molec. Formula (MF): C18 H13 Cl N4 O5 S2

Molecular Weight (MW): 464.90

Lawson Number (LN): 31458, 28769, 14131

Compound Type (CTYPE): heterocyclic

Constitution ID (CONSID): 6628019
Tautomer ID (TAUTID): 7357920
Beilstein Citation (BSO): 6-27

Entry Date (DED): 1998/03/03 Update Date (DUPD): 1998/03/03

Reference(s):

Molec. Formula (MF): C15 H13 Br N4 O5 S2

Molecular Weight (MW): 473.32

Lawson Number (LN): 31458, 28769, 2947

Compound Type (CTYPE): heterocyclic

Constitution ID (CONSID): 6627609
Tautomer ID (TAUTID): 7357341
Beilstein Citation (BSO): 6-27

Entry Date (DED): 1998/03/03 Update Date (DUPD): 1998/03/03

Reference(s):

7782314

Molec. Formula (MF):

C15 H13 C1 N4 O5 S2

Molecular Weight (MW):

428.86

Lawson Number (LN):

31458, 28769, 2947

Compound Type (CTYPE):

heterocyclic

Constitution ID (CONSID):
Tautomer ID (TAUTID):

6627686 7357707

Beilstein Citation (BSO):

6-27 1998/03/03

Entry Date (DED):
Update Date (DUPD):

1998/03/03

Reference(s):

Molec. Formula (MF): C13 H11 Br N4 O5 S2

Molecular Weight (MW): 447.28

Lawson Number (LN): 31458, 28769, 2817

Compound Type (CTYPE): heterocyclic Constitution ID (CONSID): 6622740

Tautomer ID (TAUTID): 7354727 Beilstein Citation (BSO): 6-27

Entry Date (DED): 1998/03/03 Update Date (DUPD): 1998/03/03

Reference(s):

L8 ANSWER 8 OF 8 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL on STN

Beilstein Records (BRN): 7781524

Molec. Formula (MF): C13 H11 Cl N4 O5 S2

Molecular Weight (MW): 402.83

Lawson Number (LN): 31458, 28769, 2817

Compound Type (CTYPE): heterocyclic

Constitution ID (CONSID): 6621898
Tautomer ID (TAUTID): 7355053
Beilstein Citation (BSO): 6-27

Entry Date (DED): 1998/03/03 Update Date (DUPD): 1998/03/03

Reference(s):

=> d 11; d his; log y
L1 HAS NO ANSWERS
L1 STR

Structure attributes must be viewed using STN Express query preparation.

(FILE 'HOME' ENTERED AT 15:19:02 ON 23 JUL 2003)

FILE 'REGISTRY' ENTERED AT 15:19:11 ON 23 JUL 2003

L1 STRUCTURE UPLOADED

L2 1 S L1

L3 19 S L1 FUL

FILE 'CAPLUS' ENTERED AT 15:19:42 ON 23 JUL 2003

L4 8 S L3

FILE 'BEILSTEIN' ENTERED AT 15:20:28 ON 23 JUL 2003

L5 2 S L1

L6 8 S L1 FUL

L7 8 S L6 NOT L4

L8 8 S L6 NOT L3

FILE 'MARPAT' ENTERED AT 15:21:34 ON 23 JUL 2003

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.40	454.19
DISCOUNT AMOUNTS (FOR OUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
DISCOUNT AMOUNTS (FOR QUALIFITING ACCOUNTS)	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-5.21

STN INTERNATIONAL LOGOFF AT 15:21:49 ON 23 JUL 2003